In the claims:

Please cancel claims 111-230.

Please add the following new claims.

Current listing of claims

Claims 1-230 (canceled).

231. (New) A method for identifying an atom of a common ligand mimic that is proximal to an interface region of an enzyme;

wherein the enzyme can bind a common ligand (CL) or a common ligand mimic (CL mimic) at a common ligand site (CL site) and can bind a specificity ligand (SL) at an adjacent specificity ligand site (SL site);

wherein an interface region is defined as the atoms of the enzyme between the CL site and SL site, and atoms of an SL, if bound to the enzyme;

wherein the enzyme can catalyze a reaction involving the SL and a reactive atom of the CL; and

wherein a CL reactive region is defined as CL atoms immediately adjacent to the SL;

comprising the steps of:

(a) identifying an atom of the interface region, comprising the steps of:

(1) binding an SL to the SL site of said enzyme;

(2) irradiating a nucleus of an atom of the SL reactive region; and

(3) identifying in a multidimensional NMR experiment an NMR cross-peak corresponding to a nucleus of said enzyme that is perturbed by the irradiation of the nucleus of the SL reactive region, thereby identifying an atom of the interface region; then

(b) identifying an atom in a CL mimic that is proximal to the interface region, comprising the steps of:

(1) binding a CL mimic to the CL site of said enzyme;

(2) irradiating the nucleus of the interface atom identified in step (a); and

(3) identifying in a multidimensional NMR experiment an NMR cross-peak corresponding to a nucleus of the CL mimic that is perturbed by the irradiation of the interface nucleus, thereby identifying an atom of the CL mimic that is proximal to the interface region.

232. (New) The method of claim 231, wherein the enzyme has a monomer molecular weight greater than 20 kD.

233. (New) The method of claim 232, wherein the enzyme has a monomer molecular weight greater than 35 kD.

234. (New) The method of claim 231, wherein the enzyme has a complete molecular weight greater than 50 kD.

235. (New) The method of claim 234, wherein the enzyme has a complete molecular weight greater than 100 kD.

236. (New) The method of claim 231, wherein the enzyme is from a human pathogen.

237. (New) The method of claim 231, wherein the enzyme is from bacteria.

238. (New) The method of claim 231, wherein the enzyme is a dehydrogenase.

239. (New) The method of claim 231, wherein the enzyme is a kinase.

240. (New) The method of claim 231, wherein the CL is a cofactor.

241. (New) The method of claim 240, wherein the CL is ubiquitin.

242. (New) The method of claim 240, wherein the CL is SAM (S-adenosyl methionine).

243. (New) The method of claim 240, wherein the cofactor contains a nucleotide.

244. (New) The method of claim 243, wherein the CL is NAD+.

245. (New) The method of claim 243, wherein the CL is NADH.

246. (New) The method of claim 243, wherein the CL is NADP+.

247. (New) The method of claim 243, wherein the CL is NADPH.

248. (New) The method of claim 243, wherein the CL is ATP.

249. (New) The method of claim 243, wherein the CL is ADP.

250. (New) The method of claim 231, wherein the CL is farnesyl-pyrophosphate.

251. (New) The method of claim 231, wherein the CL is geranyl-pyrophosphate.

252. (New) The method of claim 231, wherein the CL is geranyl-geranyl-pyrophosphate.

253. (New) The method of claim 231, wherein the NMR cross-peak is identified by the cross-peak undergoing an intensity or shape change.

254. (New) The method of claim 231, wherein the NMR cross-peak is identified by a relaxation effect.

255. (New) The method of claim 231, wherein the NMR cross-peak is identified by the cross-peak undergoing a chemical shift change.

256. (New) The method of claim 231, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the transfer of magnetization to protons is only to or from amide protons.

257. (New) The method of claim 231, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the detectable atoms are the NH protons of protein at an amino acid selected from the group consisting of Asn, Gln, Arg and His.

258. (New) The method of claim 231, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the detectable atoms are the methyl protons of protein specifically ^{13}C-$^{1}H_3$ labeled at an amino acid selected from the group consisting of Leu, Thr, Ile, Val, Ala and Met.

259. (New) The method of claim 231, wherein an NMR cross-peak is identified using a multidimensional multinuclear NMR method that includes a ^{1}H-^{15}N correlation.

260. (New) The method of claim 259, wherein the NMR method is a ^{1}H-^{15}N correlation and nuclear Overhauser enhancement spectroscopy experiment.

261. (New) The method of claim 231, wherein an NMR cross-peak is identified using a multidimensional multinuclear NMR method that includes a ^{1}H-^{13}C correlation.

262. (New) The method of claim 261, wherein the NMR method is an HNCA experiment.

263. (New) The method of claim 231, wherein an NMR cross-peak is identified using an NMR method that includes a $\{^{1}H,^{1}H\}$ NOESY step.

264. (New) The method of claim 263, further comprising the step of introducing a third dimension for ^{15}N or ^{13}C chemical shift.

265. (New) The method of claim 263, wherein a diagnostic ^{1}H-^{13}C or ^{1}H-^{15}N one bond coupling constant is obtained without decoupling to a heteroatom in one of the two dimensions.

266. (New) The method of claim 263, further comprising the step of using 2D ^{13}C-^{1}H or ^{15}N-^{1}H HMQC or HSQC-{^{1}H,^{1}H} NOESY.

267. (New) The method of claim 231, wherein an NMR cross-peak is identified using an NMR experiment that uses transverse relaxation-optimized spectroscopy (TROSY), whereby narrow line widths are achieved.

268. (New) The method of claim 231, wherein an NMR cross-peak is identified using an NMR experiment that uses deuterium labeling, whereby narrow line widths are achieved.

269. (New) The method of claim 231, wherein immediately adjacent is within 5 Ångstroms.

270. (New) The method of claim 231, wherein immediately adjacent is within 4 Ångstroms.

271. (New) A method for identifying an atom of a common ligand mimic that is proximal to an interface region of an enzyme;

wherein the enzyme can bind a common ligand (CL) or a common ligand mimic (CL mimic) at a common ligand site (CL site) and can bind a specificity ligand (SL) at an adjacent specificity ligand site (SL site);

wherein an interface region is defined as the atoms of the enzyme between the CL site and SL site, and atoms of an SL, if bound to the enzyme;

wherein the enzyme can catalyze a reaction involving the SL and a reactive atom of the CL; and

wherein a CL reactive region is defined as the reactive atom of the CL and CL atoms immediately adjacent to the SL;

comprising the steps of:

(a) identifying an atom of the interface region, comprising the steps of:

(1) binding a CL to the CL site of said enzyme and an SL mimic to the SL site of said enzyme, thereby forming an enzyme-CL-SL mimic complex;

(2) obtaining an NMR spectrum;

(3) binding a chemically modified CL to the CL site of the enzyme and said SL mimic to the SL site of said enzyme, wherein the modification is to an atom of the CL reactive region, and obtaining an NMR spectrum; and

(4) comparing the spectra from steps (a)(2) and (a)(3) to identify an NMR cross-peak corresponding to a nucleus that is affected by the chemical modification, thereby identifying an atom of the interface region; then

(b) identifying an atom in a CL mimic that is proximal to the interface region, comprising the steps of:

(1) binding a CL mimic to the CL site of said enzyme;

(2) irradiating the nucleus of the interface atom identified in step (a); and

(3) identifying in a multidimensional NMR experiment an NMR cross-peak corresponding to a nucleus of the CL mimic that is perturbed by the irradiation of the interface nucleus, thereby identifying an atom of the CL mimic that is proximal to the interface region.

272. (New) The method of claim 271, wherein the enzyme has a monomer molecular weight greater than 20 kD.

273. (New) The method of claim 272, wherein the enzyme has a monomer molecular weight greater than 35 kD.

274. (New) The method of claim 271, wherein the enzyme has a complete molecular weight greater than 50 kD.

275. (New) The method of claim 274, wherein the enzyme has a complete molecular weight greater than 100 kD.

276. (New) The method of claim 271, wherein the enzyme is from a human pathogen.

277. (New) The method of claim 271, wherein the enzyme is from bacteria.

278. (New) The method of claim 271, wherein the enzyme is a dehydrogenase.

279. (New) The method of claim 271, wherein the enzyme is a kinase.

280. (New) The method of claim 271, wherein the CL is a cofactor.

281. (New) The method of claim 280, wherein the CL is ubiquitin.

282. (New) The method of claim 280, wherein the CL is SAM (S-adenosyl methionine).

283. (New) The method of claim 280, wherein the cofactor contains a nucleotide.

284. (New) The method of claim 283, wherein the CL is NAD+.

285. (New) The method of claim 283, wherein the CL is NADH.

286. (New) The method of claim 283, wherein the CL is NADP+.

287. (New) The method of claim 283, wherein the CL is NADPH.

288. (New) The method of claim 283, wherein the CL is ATP.

289. (New) The method of claim 283, wherein the CL is ADP.

290. (New) The method of claim 271, wherein the CL is farnesyl-pyrophosphate.

291. (New) The method of claim 271, wherein the CL is geranyl-pyrophosphate.

292. (New) The method of claim 271, wherein the CL is geranyl-geranyl-pyrophosphate.

293. (New) The method of claim 271, wherein the NMR cross-peak is identified by the cross-peak undergoing an intensity or shape change.

294. (New) The method of claim 271, wherein the NMR cross-peak is identified by a relaxation effect.

295. (New) The method of claim 271, wherein the NMR cross-peak is identified by the cross-peak undergoing a chemical shift change.

296. (New) The method of claim 271, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the transfer of magnetization to protons is only to or from amide protons.

297. (New) The method of claim 271, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the detectable atoms are the NH protons of protein at an amino acid selected from the group consisting of Asn, Gln, Arg and His.

298. (New) The method of claim 271, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the detectable atoms are the methyl protons of protein specifically ^{13}C-$^{1}H_3$ labeled at an amino acid selected from the group consisting of Leu, Thr, Ile, Val, Ala and Met.

299. (New) The method of claim 271, wherein an NMR cross-peak is identified using a multidimensional multinuclear NMR method that includes a ^{1}H-^{15}N correlation.

300. (New) The method of claim 299, wherein the NMR method is a ^{1}H-^{15}N correlation and nuclear Overhauser enhancement spectroscopy experiment.

301. (New) The method of claim 271, wherein an NMR cross-peak is identified using a multidimensional multinuclear NMR method that includes a ^{1}H-^{13}C correlation.

302. (New) The method of claim 301, wherein the NMR method is an HNCA experiment.

303. (New) The method of claim 271, wherein an NMR cross-peak is identified using an NMR method that includes a $\{^{1}H,^{1}H\}$ NOESY step.

304. (New) The method of claim 303, further comprising the step of introducing a third dimension for ^{15}N or ^{13}C chemical shift.

305. (New) The method of claim 303, wherein a diagnostic ^{1}H-^{13}C or ^{1}H-^{15}N one bond coupling constant is obtained without decoupling to a heteroatom in one of the two dimensions.

306. (New) The method of claim 303, further comprising the step of using 2D ^{13}C-^{1}H or ^{15}N-^{1}H HMQC or HSQC-$\{^{1}H,^{1}H\}$ NOESY.

307. (New) The method of claim 271, wherein an NMR cross-peak is identified using an NMR experiment that uses transverse relaxation-optimized spectroscopy (TROSY), whereby narrow line widths are achieved.

308. (New) The method of claim 271, wherein an NMR cross-peak is identified using an NMR experiment that uses deuterium labeling, whereby narrow line widths are achieved.

309. (New) The method of claim 271, wherein immediately adjacent is within 5 Ångstroms.

310. (New) The method of claim 271, wherein immediately adjacent is within 4 Ångstroms.

311. (New) A method for identifying an atom of a common ligand mimic that is proximal to an interface region of an enzyme;

wherein the enzyme can bind a common ligand (CL) or a common ligand mimic (CL mimic) at a common ligand site (CL site) and can bind a specificity ligand (SL) at an adjacent specificity ligand site (SL site);

wherein an interface region is defined as the atoms of the enzyme between the CL site and SL site, and atoms of an SL, if bound to the enzyme;

wherein the enzyme can catalyze a reaction involving the SL and a reactive atom of the CL; and

wherein a CL reactive region is defined as the reactive atom of the CL and CL atoms immediately adjacent to the SL;

comprising the steps of:

(a) identifying an atom of the interface region, comprising the steps of:

(1) binding a CL to the CL site of said enzyme and an SL mimic to the SL site of said enzyme;

(2) irradiating a nucleus of an atom of the SL mimic;

(3) identifying in a multidimensional NMR experiment an NMR cross-peak between an atom of said CL and an atom of said SL mimic; and an NMR cross-peak between said atom of said SL mimic, or an atom proximal to said SL mimic atom, and an atom of said enzyme, thereby identifying an SL reactive region immediately adjacent to the CL and an atom of the interface region;

(b) identifying an atom in a CL mimic that is proximal to the interface region, comprising the steps of:

(1) binding a CL mimic to the CL site of said enzyme;

(2) irradiating the nucleus of the interface atom identified in step (a); and

(3) identifying in a multidimensional NMR experiment an NMR cross-peak corresponding to a nucleus of the CL mimic that is perturbed by the irradiation of the interface nucleus, thereby identifying an atom of the CL mimic that is proximal to the interface region.

312. (New) The method of claim 311, wherein the enzyme has a monomer molecular weight greater than 20 kD.

313. (New) The method of claim 312, wherein the enzyme has a monomer molecular weight greater than 35 kD.

314. (New) The method of claim 311, wherein the enzyme has a complete molecular weight greater than 50 kD.

315. (New) The method of claim 314, wherein the enzyme has a complete molecular weight greater than 100 kD.

316. (New) The method of claim 311, wherein the enzyme is from a human pathogen.

317. (New) The method of claim 311, wherein the enzyme is from bacteria.

318. (New) The method of claim 311, wherein the enzyme is a dehydrogenase.

319. (New) The method of claim 311, wherein the enzyme is a kinase.

320. (New) The method of claim 311, wherein the CL is a cofactor.

321. (New) The method of claim 320, wherein the CL is ubiquitin.

322. (New) The method of claim 320, wherein the CL is SAM (S-adenosyl methionine).

323. (New) The method of claim 320, wherein the cofactor contains a nucleotide.

324. (New) The method of claim 323, wherein the CL is NAD+.

325. (New) The method of claim 323, wherein the CL is NADH.

326. (New) The method of claim 323, wherein the CL is NADP+.

327. (New) The method of claim 323, wherein the CL is NADPH.

328. (New) The method of claim 323, wherein the CL is ATP.

329. (New) The method of claim 323, wherein the CL is ADP.

330. (New) The method of claim 311, wherein the CL is farnesyl-pyrophosphate.

331. (New) The method of claim 311, wherein the CL is geranyl-pyrophosphate.

332. (New) The method of claim 311, wherein the CL is geranyl-geranyl-pyrophosphate.

333. (New) The method of claim 311, wherein the NMR cross-peak is identified by the cross-peak undergoing an intensity or shape change.

334. (New) The method of claim 311, wherein the NMR cross-peak is identified by a relaxation effect.

335. (New) The method of claim 311, wherein the NMR cross-peak is identified by the cross-peak undergoing a chemical shift change.

336. (New) The method of claim 311, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the transfer of magnetization to protons is only to or from amide protons.

337. (New) The method of claim 311, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the detectable atoms are the NH protons of protein at an

amino acid selected from the group consisting of Asn, Gln, Arg and His.

338. (New) The method of claim 311, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the detectable atoms are the methyl protons of protein specifically ^{13}C-$^{1}H_3$ labeled at an amino acid selected from the group consisting of Leu, Thr, Ile, Val, Ala and Met.

339. (New) The method of claim 311, wherein an NMR cross-peak is identified using a multidimensional multinuclear NMR method that includes a ^{1}H-^{15}N correlation.

340. (New) The method of claim 339, wherein the NMR method is a ^{1}H-^{15}N correlation and nuclear Overhauser enhancement spectroscopy experiment.

341. (New) The method of claim 339, wherein an NMR cross-peak is identified using a multidimensional multinuclear NMR method that includes a ^{1}H-^{13}C correlation.

342. (New) The method of claim 341, wherein the NMR method is an HNCA experiment.

343. (New) The method of claim 339, wherein an NMR cross-peak is identified using an NMR method that includes a $\{^{1}H,^{1}H\}$ NOESY step.

344. (New) The method of claim 343, further comprising the step of introducing a third dimension for ^{15}N or ^{13}C chemical shift.

345. (New) The method of claim 343, wherein a diagnostic ^{1}H-^{13}C or ^{1}H-^{15}N one bond coupling constant is obtained without decoupling to a heteroatom in one of the two dimensions.

346. (New) The method of claim 343, further comprising the step of using 2D ^{13}C-^{1}H or ^{15}N-^{1}H HMQC or HSQC-{^{1}H,^{1}H} NOESY.

347. (New) The method of claim 311, wherein an NMR cross-peak is identified using an NMR experiment that uses transverse relaxation-optimized spectroscopy (TROSY), whereby narrow line widths are achieved.

348. (New) The method of claim 311, wherein an NMR cross-peak is identified using an NMR experiment that uses deuterium labeling, whereby narrow line widths are achieved.

349. (New) The method of claim 311, wherein immediately adjacent is within 5 Ångstroms.

350. (New) The method of claim 311, wherein immediately adjacent is within 4 Ångstroms.

351. (New) A method for identifying an atom of a common ligand mimic that is proximal to an interface region of an enzyme;

wherein the enzyme can bind a common ligand (CL) or a common ligand mimic (CL mimic) at a common ligand site (CL site) and can bind a specificity ligand (SL) at an adjacent specificity ligand site (SL site);

wherein an interface region is defined as the atoms of the enzyme between the CL site and SL site, and atoms of an SL, if bound to the enzyme;

wherein the enzyme can catalyze a reaction involving the SL and a reactive atom of the CL; and

wherein a CL reactive region is defined as the reactive atom of the CL and CL atoms immediately adjacent to the SL;

comprising the steps of:

(a) identifying an atom of the interface region, comprising the steps of:

(1) binding a CL mimic to the CL site of said enzyme and an SL to the SL site of said enzyme, thereby forming an enzyme-CL mimic-SL complex;

(2) obtaining an NMR spectrum;

(3) binding a chemically modified CL to the CL site of the enzyme and said SL to the SL site of said enzyme, wherein the modification is to an atom of the CL reactive region, and obtaining an NMR spectrum; and

(4) comparing the spectra from steps (a)(2) and (a)(3) to identify an NMR cross-peak corresponding to a nucleus that is affected by the chemical modification, thereby identifying an atom of the interface region; then

(b) identifying an atom in a CL mimic that is proximal to the interface region, comprising the steps of:

(1) binding a CL mimic to the CL site of said enzyme;

(2) irradiating the nucleus of the interface atom identified in step (a); and

(3) identifying in a multidimensional NMR experiment an NMR cross-peak corresponding to a nucleus of the CL mimic that is perturbed by the irradiation of the interface nucleus, thereby identifying an atom of the CL mimic that is proximal to the interface region.

352. (New) The method of claim 351, wherein the enzyme has a monomer molecular weight greater than 20 kD.

353. (New) The method of claim 352, wherein the enzyme has a monomer molecular weight greater than 35 kD.

354. (New) The method of claim 351, wherein the enzyme has a complete molecular weight greater than 50 kD.

355. (New) The method of claim 354, wherein the enzyme has a complete molecular weight greater than 100 kD.

356. (New) The method of claim 351, wherein the enzyme is from a human pathogen.

357. (New) The method of claim 351, wherein the enzyme is from bacteria.

358. (New) The method of claim 351, wherein the enzyme is a dehydrogenase.

359. (New) The method of claim 351, wherein the enzyme is a kinase.

360. (New) The method of claim 351, wherein the CL is a cofactor.

361. (New) The method of claim 360, wherein the CL is ubiquitin.

362. (New) The method of claim 360, wherein the CL is SAM (S-adenosyl methionine).

363. (New) The method of claim 360, wherein the cofactor contains a nucleotide.

364. (New) The method of claim 363, wherein the CL is NAD+.

365. (New) The method of claim 363, wherein the CL is NADH.

366. (New) The method of claim 363, wherein the CL is NADP+.

367. (New) The method of claim 363, wherein the CL is NADPH.

368. (New) The method of claim 363, wherein the CL is ATP.

369. (New) The method of claim 363, wherein the CL is ADP.

370. (New) The method of claim 351, wherein the CL is farnesyl-pyrophosphate.

371. (New) The method of claim 351, wherein the CL is geranyl-pyrophosphate.

372. (New) The method of claim 351, wherein the CL is geranyl-geranyl-pyrophosphate.

373. (New) The method of claim 351, wherein the NMR cross-peak is identified by the cross-peak undergoing an intensity or shape change.

374. (New) The method of claim 351, wherein the NMR cross-peak is identified by a relaxation effect.

375. (New) The method of claim 351, wherein the NMR cross-peak is identified by the cross-peak undergoing a chemical shift change.

376. (New) The method of claim 351, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the transfer of magnetization to protons is only to or from amide protons.

377. (New) The method of claim 351, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the detectable atoms are the NH protons of protein at an amino acid selected from the group consisting of Asn, Gln, Arg and His.

378. (New) The method of claim 351, wherein an NMR cross-peak is identified using a multidimensional multinuclear method, wherein the detectable atoms are the methyl protons of protein specifically ^{13}C-$^{1}H_3$ labeled at an amino acid selected from the group consisting of Leu, Thr, Ile, Val, Ala and Met.

379. (New) The method of claim 351, wherein an NMR cross-peak is identified using a multidimensional multinuclear NMR method that includes a ^{1}H-^{15}N correlation.

380. (New) The method of claim 379, wherein the NMR method is a ^{1}H-^{15}N correlation and nuclear Overhauser enhancement spectroscopy experiment.

381. (New) The method of claim 351, wherein an NMR cross-peak is identified using a multidimensional multinuclear NMR method that includes a ^{1}H-^{13}C correlation.

382. (New) The method of claim 351, wherein the NMR method is an HNCA experiment.

383. (New) The method of claim 351, wherein an NMR cross-peak is identified using an NMR method that includes a $\{^{1}H,^{1}H\}$ NOESY step.

384. (New) The method of claim 383, further comprising the step of introducing a third dimension for ^{15}N or ^{13}C chemical shift.

385. (New) The method of claim 383, wherein a diagnostic ^{1}H-^{13}C or ^{1}H-^{15}N one bond coupling constant is obtained without decoupling to a heteroatom in one of the two dimensions.

386. (New) The method of claim 383, further comprising the step of using 2D ^{13}C-^{1}H or ^{15}N-^{1}H HMQC or HSQC-$\{^{1}H,^{1}H\}$ NOESY.

387. (New) The method of claim 351, wherein an NMR cross-peak is identified using an NMR experiment that uses transverse relaxation-optimized spectroscopy (TROSY), whereby narrow line widths are achieved.

388. (New) The method of claim 351, wherein an NMR cross-peak is identified using an NMR experiment that uses deuterium labeling, whereby narrow line widths are achieved.

389. (New) The method of claim 351, wherein immediately adjacent is within 5 Ångstroms.

390. (New) The method of claim 351, wherein immediately adjacent is within 4 Ångstroms.